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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,641	09/09/1999	GUNTER SCHMIDT	020600-280	5378
21839	7590	06/07/2004	EXAMINER	
BURNS DOANE SWECKER & MATHIS L L P			FORMAN, BETTY J	
POST OFFICE BOX 1404			ART UNIT	
ALEXANDRIA, VA 22313-1404			PAPER NUMBER	
			1634	
DATE MAILED: 06/07/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
09/341,641	SCHMIDT ET AL.	
Examiner	Art Unit	
BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Response

- 1) ☐ Responsive to communication(s) filed on ____.
- a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-39 and 41-43 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 21-39 and 41-43 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Specification Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 January 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)

Paper No(s)/Mail Date 7/00, 1/03.

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Notice to Comply w/ Sequence Rules

DETAILED ACTION

Status of the Claims

1. Prosecution on the merits of this application is reopened on claims 21-39 and 41-43 considered unpatentable for the reasons indicated below:

The rejections in the Office Action of 4 December 2003, not reiterated below, are withdrawn in view of further consideration and/or new grounds for rejection. New grounds for rejection are discussed below.

Claims 21-39 and 41-43 are currently under prosecution.

Specification

2. The disclosure is objected to because of the following informalities:

a) This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

b) The specification does not contain the required heading, "BRIEF DESCRIPTION OF THE DRAWINGS" on page 5.

c) The specification contains numerous nucleic acid sequences not identified with a SEQ ID NO: (see e.g. pages 23-25).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

35 U.S.C. 112: First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In papers filed 9 June 2003, the recitations "without spatial **separation**" and "present in a unique amount" were added to the independent Claim 1. However, the specification fails to define or provide any disclosure to support such claim recitation. The specification, page 7, line 22, teaches detection without spatial **resolution**. The specification does not teach or describe analysis without spatial separation. The instantly claimed spatial separation describes the physical relationship between DNA molecules. In contrast, the spatial resolution taught in the specification describes methods of optical detection, not physical relationships. Additionally, the specification fails to describe the meets and bounds of the newly claimed "unique amount". Applicant has not pointed to support in the specification for the newly added amendment and a reading of the specification has not revealed any such support. Hence, the specification does not teach or describe the newly claimed "spatial separation" or "unique amount".

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE*

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RASMUSSEN, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE" (emphasis added).

35 U.S.C. 112: Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21-39 and 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 21-32 are indefinite in Claim 21, line 5 for the recitation "the plurality of single stranded DNA molecules" because it is unclear whether the recitation refers to the "heterogeneous population" of line 1 or some other DNA molecules. It is suggested that the claim be amended to clarify e.g. replace "plurality" with "population".

b. Claims 21-32 are indefinite in Claim 21, line 7 for the recitation "the array containing all possible base sequences being incapable of ligation to each other" because the recitation lacks proper antecedent basis in the claim. The recitation is further indefinite because it is unclear how (or whether) the array functions within the context of the method steps. It is

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suggested that the claim be amended to provide proper antecedent basis and/or describe steps utilizing the array.

c. Claims 21-32 are indefinite in Claim 21, lines 9-12 for the recitation "to ligate the double stranded portion of each DNA molecule, the probe bearing the basethereby to form an extended double stranded portion" because it is unclear what is ligated to form the extended portion.

d. Claims 21-32 are indefinite in Claim 21 because the claim is drawn to sequencing....DNA molecules simultaneously". However, the claim does not recite a method step of simultaneous detection. Furthermore, the last step (f) requires repetition of the steps a-e (i.e. contacting, removing, cleaving, recording and activating) to determine the sequence of each molecule. Hence, in contrast to the claimed "simultaneous", the method steps require multiple and repeated steps of sequence analysis.

e. Claims 21-32 are indefinite in Claim 21, step c for the recitation "the ligated probes" because the recitation lacks proper antecedent basis in the claim.

f. Claims 21-32 are indefinite in Claim 21, step d for the recitation "the quantity" because the recitation lacks proper antecedent basis in the claim.

g. Claim 22 is indefinite because it is unclear how the "sub-arrays" differ from the array. The claim defines the sub-arrays as containing all possible base sequences and each sub-array is contacted with the DNA population. However, the array of Claim 21 contains all possible base sequences. Hence it is unclear how the sub-arrays differ from the array. Claim 22 does not require a step of contacting each individual sub-array with the DNA as individual method steps. The claim merely describes the composition of the array and sub-arrays

h. Claim 23 is indefinite for the recitation "the target DNA population" because the recitation lacks proper antecedent basis in the "heterogeneous population" of Claim 21.

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i. Claim 24 is indefinite for the recitation "the initial DNA sample" because the recitation lacks proper antecedent basis in the "heterogeneous population" of Claim 21.

j. Claim 26 is indefinite for the recitation "the quantity of each label" because the recitation lacks proper antecedent basis in the probes of Claim 21.

k. Claims 33-39 and 42-43 are indefinite in Claim 33 because the claim is drawn to a kit comprising an array of probes and "means for resolving a measured quantity of a hybridized probe". However, it is unclear the "means" further limits the structural limitations/composition of the kit. The claimed "means" encompasses any number of elements e.g. microscope, computer. However, it is unclear whether these elements would be components in a kit.

l. Claim 42 is indefinite because the claim is drawn to the kit of Claim 33 wherein the means comprises an algorithm. However, the algorithm does not describe structural components and/or elements that further limit the kit. Therefore, it is unclear what limitations are being imposed upon the kit.

m. Claim 43 is indefinite because the claim is drawn to the kit of Claim 33 wherein the means comprises a computer program. However, the computer program does not describe structural components and/or elements that further limit the kit. Therefore, it is unclear what limitations are being imposed upon the kit.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 21-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Southern et al (WO 95/04160, published 9 February 1995).

Regarding Claim 21, Southern teaches a method for sequencing a single stranded DNA molecules, the DNA having a primer to provide a double stranded portion (Fig. 4-5), the method comprising contacting the DNA with hybridization probes comprising a label cleavably attached to a known base sequence of known length, the contacting being in the presence of a ligase to thereby ligate the double stranded portion to a probe complementary to the DNA to form an extended double stranded portion, removing un-ligated probes, cleaving to release the label, recording the quantity of the label, activating the extended portion to enable ligation and repeating the steps of contacting, cleaving and activating to determining the sequence of DNA molecules (page 15, line 20-page 17, line 5). Furthermore, Southern specifically teaches method simultaneously sequences a plurality of different sequences (page 17, lines 1-5). And Southern teaches the method wherein the sequencing is without spatial separation i.e. the tags are cleaved and detected (page 16, lines 5-10).

Because the tags are cleaved, the sequencing is performed without spatial separation of the tags (e.g. Example 18, pages 45-46). The instantly claimed "unique amount" is given its broadest reasonable interpretation consistent with the specification wherein it is not described and consistent with the claim wherein the uniqueness of the amount is not defined. As such, the "unique amount" can be interpreted as each DNA molecule has a unique amount (e.g. one spot of vector sequence), but not different from the amount of other DNA molecules.

Given the broadest reasonable interpretation of the claims, Southern teaches the claimed invention.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55,

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44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Regarding Claim 22, Southern teaches the method wherein an array (plurality) of probes comprising all possible n-mers are contacted with DNA (page 15, lines 28-34).

Regarding Claim 23, Southern teaches the method wherein the target DNA is obtained by sorting the DNA into sub-populations and selected one as a target e.g. DNA clones are hybridized to primers (sorted) and immobilized DNA molecules are sequenced (e.g. page 17, lines 24-31).

Regarding Claim 24, Southern teaches the method wherein the DNA is fragmented to have sticky ends of known length which are sorted onto subpopulations according to their sticky ends (Fig. 5).

Regarding Claim 25, Southern teaches the method wherein each DNA is immobilized at one end i.e. via hybridization to immobilized primer (Fig. 5).

Regarding Claim 26, Southern teaches the method wherein the label comprises a mass label and the quantity of the label is recorded using a mass spectrometer after label release (page 14 and Fig. 1-4).

Regarding Claim 27, Southern teaches the method wherein the known base is blocked at the 3' OH (page 16, lines 10-25 and Fig. 4).

Regarding Claim 28, Southern teaches the method wherein the cleaving unblocks the 3' OH of the extended double stranded portion (page 16, lines 10-25 and Fig. 4).

Regarding Claim 29, Southern teaches the method wherein the label of each probe is cleavable attached to the 3' OH (page 16, lines 10-25 and Fig. 4).

Regarding Claim 30, Southern teaches the method wherein the probe is unphosphorylated at the 3' and 5' ends and the method comprises phosphorylating the 5' OH of the extended double stranded portion (page 16, lines 10-25 and Fig. 4).

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Regarding Claim 31, Southern teaches the method wherein the predetermined length is from 2 to 6 (page 2, lines 1-8 and Claim 4).

Regarding Claim 32, Southern teaches the method wherein the predetermined length is 4 (page 2, lines 1-8 and Claim 4).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 32-39, 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (WO 95/04160, published 9 February 1995) and Drmanac (WO 95/09248, published 6 April 1995) and Stratagene (catalog, 1989, page 39)

Regarding Claim 32, Southern teaches an array of probes, each comprising a label cleavable attached to a known base and having a predetermined length, the array comprising all possible base sequences of that length and means for resolving a measured quantity e.g. detectable mass label (Claims 12) but they do not specifically teach the array in kit format. However, Drmanac teaches a similar array wherein the array is provided in kit format comprising all components for sequencing target DNA (page 17, line 24-page 18, line 15).

Furthermore, Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

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It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Southern into a kit format as taught by Drmanac and as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Regarding Claim 34, Southern teaches the method wherein the known base is blocked at the 3' OH (page 16, lines 10-25 and Fig. 4).

Regarding Claim 35, Southern teaches the method wherein the label of each probe is cleavable attached to the 3' OH (page 16, lines 10-25 and Fig. 4).

Regarding Claim 36, Southern teaches the method wherein the probe is unphosphorylated at the 3' and 5' ends and the method comprises phosphorylating the 5' OH of the extended double stranded portion (page 16, lines 10-25 and Fig. 4).

Regarding Claim 37, Southern teaches the method wherein the label comprises a mass label (page 14 and Fig. 1-4).

Regarding Claim 38, Southern teaches the method wherein the predetermined length is from 2 to 6 (page 2, lines 1-8 and Claim 4).

Regarding Claim 39, Southern teaches the method wherein the predetermined length is 4 (page 2, lines 1-8 and Claim 4).

Regarding Claim 41, Southern teaches the method of using the components of the kit comprising contacting target DNA with the array of probes, cleaving labels from the probes to identify the probes and determining the sequence of the DNA from the identity of the probes (page 15, line 20-page 17, line 5).

Regarding Claims 42 and 43, the claims are drawn to the kit of Claim 33 wherein the means comprise an algorithm or computer program. However, the algorithm and computer

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program do not define or describe structural components to further limit the kit product.

Hence, the algorithm and computer program do not further limit the kit. However, it is noted that Southern teaches measurement of the tag which requires measuring algorithm.

Furthermore, Drmanac teaches a computer program/algorithm for analysis of the sequencing reactions (page 11, line 36-page12, line 14. Hence, the prior art teaches the non-structural components recited in the claims.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." *Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114).

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18, 20-24, 27 and 28

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of copending Application No. 09/462,408. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of sequence analysis and differ only in the arrangement of the limitations within the claim sets. For example, instant Claim 21 requires ligase and ligation while dependent Claim 13 of the '408 application is drawn to ligation. Hence, the claim sets are drawn to methods which are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

NOTICE TO COMPLY WITH NUCLEIC ACID SEQUENCE RULES

13. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS A PERIOD OF TIME CO-EXTENSIVE WITH THE TIME TO REPLY TO THE ABOVE OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

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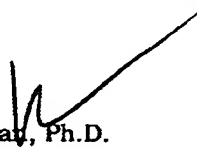
Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
June 2, 2004